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EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,443	EATON ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

2. Applicant's submission filed on 22 June 2006 has been entered. Claims 1-27 and 40-52 were previously cancelled. Claim 28 has been amended. Claims 28-39 are under prosecution.

3. The previous rejections under 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 28 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilvert et al (U.S. Patent No. 5,208,152, issued 4 May 1993) in view of Ellington et al (Nature, vol. 355, pages 850-852 (1992)).

Regarding claim 28, Hilvert et al teach a method for producing a cyclohexene derivative product library comprising

contacting a mixture of different first reactants (e.g., a racemic mixture of a dienophile; column 26, lines 25-30) each coupled to a member of a test mixture (e.g., the dienenophiles and dienes bind to an antibody that catalyzes a Diels-Alder reaction; Abstract) with a mixture of different free reactants (e.g., a racemic mixture of dienes; column 26, lines 25-30), wherein:

each said first reactant is a dienophile and each said free reactant is a diene, or each said first reactant is a diene and each said free reactant is a dienophile (e.g., the dienenophiles and dienes bind to an antibody that catalyzes a Diels-Alder reaction; Abstract).

With respect to contacting a mixture of different free reactants to a mixture of first reactants each coupled to a member of the test mixture, the limitation "coupled" is interpreted as noncovalent binding of a reactant to an antibody catalyst; thus, the claim has been given the broadest reasonable interpretation consistent with the specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]). Therefore, the coupling of the first reactant to the test mixture and the contacting of the coupled mixture with the free reactant is interpreted as mixing of the three species in the order listed.

While Hilvert et al do not teach mixing the first reactants with the test mixture followed by mixing with the free reactants, the courts have held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). See MPEP 2144.04 IV.C. Therefore, the instantly claimed contacting of a mixture of first reactants coupled to a test mixture with a mixture of free reactants is an obvious variant of the order of admixing a dienophile and diene with a catalyst as taught by Hilvert et al (column 24, lines 9-25).

Hilvert et al also teach said product library comprises a mixture of products (e.g., diastereomeric cyclic reaction products are formed; column 26, lines 21-30) that is formed as a result of a Diels-Alder bond formation reaction between said first reactants and said free reactants, wherein said Diels-Alder bond formation reaction is facilitated by the test mixture coupled to said first reactant (Abstract and column 24, lines 9-25), and that it would be beneficial to find specific catalysts for Diels-Alder reactions (column 5, lines 15-17).

Hilvert et al do not teach the test mixture is nucleic acids.

However, Ellington et al teach a method of obtaining single-stranded DNA molecules capable of ligand binding that are isolated via selection and amplification in vitro (Abstract, lines 1-4) that are analogous to catalytic antibodies (page 852, column 2, last paragraph) with the added advantage that nucleic acid aptamers are new catalysts for chemical transformations with a preference for transition-state binding as opposed to product or substrate binding (page 852, column 2, last paragraph).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the method comprising using catalytic antibodies for Diels-Alder reactions as taught by Hilvert et al with the ligand binding nucleic acids as taught by Ellington et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in providing new catalysts for chemical transformations with a preference for transition-state binding as opposed to product or substrate binding that are analogous to catalytic antibodies as taught by Ellington et al (page 852, column 2, last paragraph).

Regarding claim 32, the method of claim 28 is discussed above. Ellington et al also teach the use of DNA oligomers having a region of conserved sequences (e.g., defined primer-binding sites; page 850, column 1, paragraph 2, lines 2-3) and a region of randomized sequences (page 850, column 1, paragraph 2, lines 1-2).

Regarding claim 33, the method of claim 28 is discussed above. Ellington et al teach the use of single-stranded DNA (page 850, column 1, paragraph 2, lines 4-6), and that the methods are similar to those used for RNA (Abstract, lines 1-4).

Regarding claims 34 and 35, the method of claim 28 is discussed above. As noted above, the coupling of the first reactant to the test mixture is interpreted as noncovalent binding of a reactant to a catalyst; thus, the claim has been given the broadest reasonable interpretation consistent with the specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]). Therefore, the coupling of the first reactant to the test mixture and the contacting of the coupled mixture with the free reactant is interpreted as mixing of the three species in the order listed.

While Hilvert et al do not teach explicitly teach which of the diene or dienophile is first coupled to the catalyst, the courts have held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). See MPEP 2144.04 IV.C. Therefore, the limitations on the order of operations required by claims 34 and 35 (i.e., coupling either the diene of the dieneophile with the catalyst first) are obvious variants of the order of admixing a dienophile and diene with a catalyst as taught by Hilvert et al (column 24, lines 9-25).

3. Claims 29 and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilvert et al (U.S. Patent No. 5,208,152, issued 4 May 1993) in view of Ellington et al (Nature, vol. 355, pages 850-852 (1992)) as applied to claim 28 above, and further in view of Verdine (PCT International Publication Number WO 93/14108, published 22 July 1993).

Regarding claim 29, the method of claim 28 is discussed above. Neither Hilvert et al nor Ellington et al teach the use of linker groups.

However, Verdine teaches the use of linker groups between nucleic acids and first reactants (e.g., a reversible bond between a target deoxyribonucleic acid and a specific binding molecule [i.e., a peptide];

page 5, lines 4-23) with the added advantage that the linker group (i.e., reversible bond) permits the release of the specific binding molecule (i.e., the peptide) according to its DNA association constant (page 5, lines 24-34)

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the method comprising first reactants coupled to nucleic acids as taught by Hilvert et al and Ellington et al with the linker between the first reactant and the nucleic acid as taught by Verdine with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in permitting the release of the first reactant (i.e., specific binding molecule) according to its deoxyribonucleic acid association constant as explicitly taught by Verdine (page 5, lines 24-34).

Regarding claim 36, the method of claim 28 is discussed above. Neither Hilvert et al nor Ellington et al teach functional groups on the test mixture.

However, Verdine teaches the attachment of functional groups (e.g., multidentate ligands, page 10, line 32) including substituted thiols and substituted carboxylic acids (page 11) to the test mixture (e.g., deoxyribonucleic acids; page 7, lines 12-13 and Figure 1) with the added advantage that said functional groups are used to design and synthesize molecules which specifically bind a desired deoxyribonucleic acid sequence (page 8, lines 1-5).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the method comprising first reactants coupled to nucleic acids as taught by Hilvert et al and Ellington et al with the functional groups on the deoxyribonucleic acid test mixture as taught by Verdine with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in allowing the design and synthesis of molecules which specifically bind a desired deoxyribonucleic acid sequence as explicitly taught by Verdine (page 8, lines 1-5).

Regarding claim 37, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a ribose position of said nucleic acid (e.g., the 5' or 3' carbons; page 16, line 31-page 17, line 2).

Regarding claim 38, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a base of said nucleic acid (page 16, lines 31-32).

Regarding claim 39, the method of claim 36 is described above. Verdine also teaches the attachment of the functional group on a phosphate position of said nucleic acid (e.g., at internucleotide phosphorous atoms; page 17, lines 1-2).

4. Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hilvert et al (U.S. Patent No 5,208,152, issued 4 May 1993), Ellington et al (Nature, 1992: 355, pp. 850-852) and Verdine (PCT International Publication Number WO 93/14108, published 22 July 1993) as applied to claim 29 above, and in further view of Cload et al (J. Am. Chem. Soc., 1993, 115, pp 5005-5014) as evidenced by Jolly (Modern Inorganic Chemistry, 1984, McGraw Hill).

Regarding claims 30 and 31, the method of claim 29 is discussed above. Neither Hilvert et al, Ellington et al, nor Verdine teach the use of linker groups having a size in the range of 10 to 1000 Angstroms.

However, Cload et al teach the use of test nucleic acids with linker groups in the size range of 10 to 1000 Angstroms (e.g., oligonucleotide probes tethered with a neutral polyethylene glycol linker; page 5006, column 1, paragraph 2, lines 4-6). Jolly et al define the average C-C bond length as 1.54 Angstroms (Tables 3.5 and 3.6, page 52); therefore, the linkers of Cload et al are between 10 and 1000 Angstroms. Cload et al also teach that the linker has the added advantage of minimizing possible electrostatic effects (page 5006, column 1, paragraph 2, lines 4-6).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the method comprising first reactants coupled to nucleic acids as

taught by Hilvert et al, Ellington et al, and Verdine with the linker groups as taught by Cload et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in linkers that minimize possible electrostatic effects as explicitly taught by Cload et al (page 5006, column 1, paragraph 2, lines 4-6).

Response to Arguments

Applicant's arguments filed 22 June 2006 (i.e., "the Remarks") have been fully considered but they are not persuasive for the reason(s) given below.

1. Applicant argues on pages 6-8 of the Remarks that Ellington et al and Hilvert et al (the '152 patent) do not teach either a product library comprised of a mixture of different products or a mixture of different free reactants.

However, Hilvert et al do in fact teach a mixture of different first reactants (e.g., a racemic mixture of a dienophile; column 26, lines 25-30) and a mixture of different free reactants (e.g., a racemic mixture of dienes; column 26, lines 25-30) to produce a product library comprising a mixture of products (e.g., diastereomeric cyclic reaction products are formed; column 26, lines 21-30).

2. Applicant argues on page 7 of the Remarks that Ellington et al teaches three separate mixtures of nucleic acids, and that the diversity of the library of Ellington et al is only in the sequences of the nucleic acid ligands. These arguments have been considered but are moot in view of the new rejections necessitated by the amendments; i.e., the new rejections rely on the diversity of the library as taught by Hilvert et al, not Ellington et al.

3. Applicant also argues on page 7 of the Remarks that the Ellington et al suggest that nucleic acid ligands may be able to serve as catalysts for subsequent reactions, but that Ellington et al do not provide any suggestion or guidance as to the type of reactions that may be catalyzed by the nucleic acid ligands.

However, Ellington et al clearly suggest the use of DNA nucleic acids for use in chemical transformations (page 852, column 2, last paragraph). In addition, Ellington et al teach that RNA nucleic acids catalyze chemical transformations (page 852, column 2, last paragraph). As Applicant acknowledges in paragraph 3 on page 8 of the Remarks, it would have been obvious to a person or ordinary skill in the art at the time the invention was made to use the nucleic acid aptamers as taught by Ellington et al to identify a catalyst for an chemical transformation. Hilvert et al teaches that that it would be beneficial to find specific catalysts for Diels-Alder reactions (column 5, lines 15-17). Thus, the obviousness of modifying the teachings of Hilvert et al with the teachings of Ellington et al is found in both references; i.e., Hilvert et al teach the need of a Diels-Alder catalyst, and Ellington et al teach potential source of catalysts for reactions, using either nucleic acids with established catalytic properties (e.g., RNA) or potential catalytic properties (e.g., DNA).

In addition, the new claim limitations requiring the mixture of different free reactants and the mixture of products in the product library are addressed in the new rejections necessitated by the amendments.

Finally, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

4. Applicant also argues on page 8 of the Remarks that Hilvert et al merely teaches an antibody capable of catalyzing one specific type of Diels-Alder reaction. However, Hilvert et al teach that the use of the catalyst with reactant dienes and dienophiles that are preferably substituted with one or more substituent groups (column 5, lines 43-51; emphasis added). In addition, Hilvert et al teach a mixture of different first reactants (e.g., a racemic mixture of a dienophile; column 26, lines 25-30) and a mixture of different free reactants (e.g., a racemic mixture of dienes; column 26, lines 25-30) to produce a product

library comprising a mixture of products (e.g., diastereomeric cyclic reaction products are formed; column 26, lines 21-30). Therefore, Hilvert et al teach the catalyst is able to catalyze the many different types of Diels-Alder reactions required to produce the plurality of products from the plurality of reactants described above.

5. The arguments on pages 8-9 of the Remarks regarding the alleged deficiencies of Woo et al have been considered but are moot in view of the new rejections necessitated by the amendments.

6. The remaining arguments on pages 8-10 of the Remarks rely on arguments set forth to address the alleged deficiencies of Hilvert et al and Ellington et al. Since the arguments regarding Hilvert et al and Ellington et al were not persuasive, the rejections of the dependent claims are maintained.

Conclusion

1. No claim is allowed.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634

JULIET C. SWITZER
PRIMARY EXAMINER